



Abstracts

Articles appearing in the October 2018 issue

Everolimus for treatment-refractory seizures in TSC: Extension of a randomized controlled trial

Background EXamining everolimus In a Study of Tuberous sclerosis 3 (EXIST-3) demonstrated significantly reduced seizure frequency (SF) with everolimus vs placebo. In this study, we evaluate the long-term efficacy and safety of everolimus for tuberous sclerosis complex (TSC)-associated treatment-refractory seizures.

Methods After completion of the core phase, patients could enter an open-label extension phase and receive everolimus (target exposure, 3–15 ng/mL) for ≥ 48 weeks. Efficacy end points included change from baseline in average weekly SF expressed as response rate (RR, $\geq 50\%$ reduction) and median percentage reduction (PR).

Results Of 366 patients, 361 received everolimus in core/extension phases. The RR was 31% (95% CI, 26.2–36.1; N = 352) at week 18, 46.6% (95% CI, 40.9–52.5; N = 298) at 1 year, and 57.7% (95% CI, 49.7–65.4; N = 163) at 2 years. Median PR in SF was 31.7% (95% CI, 28.5–36.1) at week 18, 46.7% (95% CI, 40.2–54) at 1 year, and 56.9% (95% CI, 50–68.4) at 2 years. Ninety-five patients (26.3%) discontinued everolimus before 2 years; 103 (28.5%) had < 2 years of follow-up at study cutoff, and 40% were exposed to everolimus for ≥ 2 years. An analysis classifying discontinued patients as nonresponders showed an RR of 30.2% (95% CI, 25.5–35.2; N = 361) at week 18, 38.8% (95% CI, 33.7–44.1; N = 358) at 1 year, and 41% (95% CI, 34.6–47.7; N = 229) at 2 years, suggesting sustained benefit over time. The incidence of grade 3/4 adverse events (AEs) (any cause) was 40.2%, and 13% discontinued because of AEs (pneumonia [1.7%] and stomatitis [1.4%]). Two deaths were suspected to be treatment-related (pneumonia and septic shock).

Conclusions Sustained reductions in TSC-associated treatment-refractory seizures over time were achieved with adjunctive everolimus. The safety profile was consistent with the core phase with no new safety concerns.

Classification of evidence This study provides Class IV evidence that long-term everolimus therapy reduces SF in patients with TSC-associated treatment-refractory seizures.

NPub.org/NCP/9302a

Presentation, etiology, and outcome of brain infections in an Indonesian hospital: A cohort study

Background Little detailed knowledge is available regarding the etiology and outcome of CNS infection, particularly in HIV-infected individuals, in low-resource settings.

Methods From January 2015 to April 2016, we prospectively included all adults with suspected CNS infection in a referral hospital in Jakarta, Indonesia. Systematic screening included HIV testing, CSF examination, and neuroimaging.

Results A total of 274 patients with suspected CNS infection (median age 26 years) presented after a median of 14 days with headache (77%), fever (78%), seizures (27%), or loss of consciousness (71%). HIV coinfection was common (54%), mostly newly diagnosed (30%) and advanced (median CD4 cell count 30/ μ L). Diagnosis was established in 167 participants (65%), including definite tuberculous meningitis (TBM) (n = 44), probable TBM (n = 48), cerebral toxoplasmosis (n = 48), cryptococcal meningitis (n = 14), herpes simplex virus/varicella-zoster virus/cytomegalovirus encephalitis (n = 10), cerebral lymphoma (n = 1), neurosyphilis (n = 1), and mucormycosis (n = 1). In-hospital mortality was 32%; 6-month mortality was 57%. The remaining survivors had either moderate or severe disability (36%) according to Glasgow Outcome Scale.

Conclusion In this setting, patients with CNS infections present late with severe disease and often associated with advanced HIV infection. Tuberculosis, toxoplasmosis, and cryptococcosis are common. High mortality and long-term morbidity underline the need for service improvements and further study.

NPub.org/NCP/9302b

Practice Current

Neurology: Clinical Practice has launched their next Practice Current survey on a universally challenging topic: “How do you diagnose and treat post-concussive headache?” Please consider completing the survey to add your own perspective. In the June 2019 issue, readers will have access to opinions from David W. Dodick, MD (US), Mohammad Wasay, MBBS, MD, FRCP (Pakistan), and Karen M. Barlow, MSc, MBChB, MRCPCH, RACP (Australia).

NPub.org/NCP/pc09

Neurology®

What's happening in *Neurology*® *Clinical Practice*
Neurology 2019;93;63
DOI 10.1212/WNL.00000000000007752

This information is current as of July 8, 2019

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/93/2/63.full
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2019 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

